

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1 (currently amended) A method for the simultaneous quantitative analysis of at least three samples of molecules, wherein the molecules are derivatized prior to analysis, comprising:

- (i) reacting the molecules of each sample with at least two differential isotope labeled reagents, wherein the reagents are directly labeled without use of an affinity group, and wherein the differential isotope labeled reagents result in differential isotope labeled derivatives of the molecules;
- (ii) combining the derivatives of the molecules for examination by mass spectrometry; and
- (iii) examining the derivatives of the molecules by mass spectrometry.

Claim 2 (currently amended) A method for the quantitative analysis of a sample of molecules, wherein the molecules have an amine bearing an active hydrogen and wherein the molecules are derivatized prior to analysis, ~~having an amine bearing an active hydrogen~~, comprising:

- (i) reacting the molecules with ~~differential~~ isotope labeled reagents, wherein the reagents are directly labeled without use of an affinity group, and wherein reaction with the differential isotope labeled reagents result results in a reductive alkylation of the amine of the molecules to its-alkylamine derivative derivatives of the molecules, such that the alkylamine ~~derivative is~~ derivatives are isotopically labeled for examination by mass spectrometry; and
- (ii) examining the ~~derivative~~ derivatives of the molecules by mass spectrometry.

Claim 3 (currently amended) A method for the quantitative analysis of two or more samples of molecules, wherein the molecules have an amine bearing an active hydrogen

and the molecules are derivatized prior to analysis, having an amine bearing an active hydrogen, comprising:

- (i) reacting the molecules in each sample with differential isotope labeled reagents, wherein the reagents are directly-labeled without use of an affinity group, and wherein the differential isotope labeled reagents result in a reductive alkylation of the amine of the molecules to its alkylamine derivative derivatives of the molecules, such that the alkylamine derivatives of each sample are differential isotope are differentially isotopically-labeled;
- (ii) combining the derivatives of the molecules for examination by mass spectrometry; and
- (iii) examining the derivatives of the molecules by mass spectrometry.

Claim 4 (currently amended) The method of any of claims claim 1, 2 or 3 comprising an additional step of cleaving the derivatives into fragments, prior to the step of examining the derivatives by mass spectrometry.

Claim 5 (currently amended) The method of any of claims claim 1, 2 or 3 comprising an additional step of denaturing the molecules prior to the step of reacting the molecules with differential isotope labeled reagents.

Claim 6 (currently amended) The method of any of claims claim 1, 2, or 3 or 4 wherein the step of examining the derivatives by mass spectrometry comprises introducing the derivatives or fragments to a mass spectrometer using electrospray ionization.

Claim 7 (currently amended) The method of claim 6 wherein the electrospray ionization method is selected from [[a]] the group consisting of nanospray, pneumatically assisted electrospray, ionspray and turboionspray.

Claim 8 (currently amended) The method of any of claims claim 1, 2 or 3 comprising an additional step of separating the derivatives before the step of examining the derivatives by mass spectrometry.

- Claim 9 (currently amended) The method of claim 8 wherein the step of separating the derivatives uses a separator selected from [[a]] the group consisting of 1-D gel electrophoresis, SDS-PAGE, isoelectric focusing, 2-D gel electrophoresis, zone electrophoresis, isotachopheresis, ion exchange chromatography, normal phase chromatography, reverse phase chromatography, hydrophobic interaction chromatography, size exclusion chromatography and any combination of these separators.
- Claim 10 (Previously presented) The method of claim 4 comprising an additional step of separating the fragments after the step of cleaving the derivatives and before the step of examining the derivatives.
- Claim 11 (original) The method of claim 10 wherein the step of separating the fragments uses a separator selected from [[a]] the group consisting of liquid chromatography, high performance liquid chromatography and capillary electrophoresis.
- Claim 12 (currently amended) The method of any of claims ~~claim~~ 1, 2 or 3 comprising an additional step of analyzing the derivatives after the step of examining the derivatives by mass spectrometry.
- Claim 13 (currently amended) The method of claim 12 wherein the derivatives are peptides and the step of analyzing the derivatives is selected from [[a]] the group consisting of collision-induced dissociation in a mass spectrometer operating in MS/MS mode, peptide mass fingerprinting, peptide mapping, Edman sequencing and sequencing by sequential amino acid cleavage.
- Claim 14 (Previously presented) The method of claim 13, comprising an additional step, after the step of analyzing the derivatives, of sequencing the molecule.
- Claim 15 (currently amended) The method of any of claims ~~claim~~ 1, 2 or 3 wherein the differential isotope labeled reagents are an aldehyde and a reducing agent.
- Claim 16 (currently amended) The method of claim 15 wherein the aldehyde is selected from [[a]] the group consisting of formaldehyde and acetaldehyde.

- Claim 17 (currently amended) The method of claim 15 wherein the reducing agent is selected from [[a]] the group consisting of a sodium cyanoborohydride, sodium borohydride, dialkyl borane complexes and pyridine borane complexes.
- Claim 18 (currently amended) The method of any of claims ~~claim~~ 1, 2 or 3 wherein the sample in any one of claim 1, 2 or 3 is selected from [[a]] the group consisting of cells, cellular extracts, sub-cellular extracts, cellular lysates, peptides, proteins, drugs, toxins, antibodies and pollutants.
- Claim 19 (currently amended) The method of claim 18 wherein the sample comprises a protein having an amine and the protein is ~~proteins are~~ extracted from a cell ~~cells~~.
- Claim 20 (currently amended) The method of claim 19 wherein the amine of the protein ~~proteins~~ is selected from [[a]] the group consisting of a lysine residue, ornithine residue and a residue at the N- terminal amino group of the protein ~~proteins~~.
- Claim 21 (currently amended) The method of any of claims ~~claim~~ 1, 2 or 3 wherein the step of examining the derivatives of the molecules by mass spectrometry utilizes a mass spectrometer selected from [[a]] the group consisting of:
- (i) Fourier transform – Ion cyclotron resonance mass spectrometers (FT-ICR-MS);
 - (ii) Time of Flight mass spectrometers (TOF-MS, TOF-TOF-MS);
 - (iii) Ion trap mass spectrometers (IT);
 - (iv) Quadrupole mass spectrometers (Q-MS and QqQ-MS);
 - (v) Ion mobility mass spectrometers (IM-MS);
 - (vi) Quadrupole (or hexapole, octapole)-Time of Flight mass spectrometers (Q-TOF, and Qq-TOF); and
 - (vii) Ion trap – Time of flight mass spectrometers (IT-TOF).
- Claim 22 (Previously presented) The method of claim 21 comprising an additional step of combining the mass spectrometer with an ionization source.

Claim 23 (currently amended) The method of claim 22 wherein the ionization source is selected from ~~[[a]]~~ the group consisting of electrospray ionization, matrix-assisted laser desorption and ionization (MALDI), field desorption, thermal desorption and laser desorption.

Claim 24 (currently amended) A preparation comprising three samples of derivatives of molecules for simultaneous quantitative analysis by mass spectrometry, each sample comprising isotopically labeled derivatives of molecules, each sample resulting from a reaction of at least two differential isotope labeled reagents with the molecules, wherein the reagents are ~~directly~~ labeled without the use of an affinity group.

Claim 25 (currently amended) A preparation of a sample comprising ~~a sample of~~ isotopically labeled derivatives of molecules for quantitative analysis by mass spectroscopy, the derivatives of molecules having an amine bearing an active hydrogen, comprising isotopically labeled derivatives resulting from a reductive alkylation of the molecules, wherein the molecules have an amine bearing an active hydrogen, amine to its to alkylamine derivatives of the molecules, by isotopically labeled reagents, derivative by differential isotope labeled reagents, wherein the reagents are ~~directly~~ labeled without the use of an affinity group.

Claim 26 (currently amended) A preparation comprising two or more samples of differential isotopically labeled derivatives of molecules ~~having an amine bearing an active hydrogen, for the simultaneous~~ for quantitative analysis by mass spectrometry, ~~each sample comprising the differential~~ isotopically labeled derivatives of molecules resulting from a reductive alkylation of the molecules, wherein the molecules have an amine bearing an active hydrogen, to its alkylamine derivative by differential isotope labeled reagents, wherein the reagents are ~~directly~~ labeled without use of an affinity group.

Claim 27 (currently amended) Use of a mass spectrometer for the simultaneous analysis of at least three samples of molecules, wherein the molecules are derivatized prior to analysis, comprising:

(i) reacting the molecules of each sample with at least two differential isotope labeled reagents, wherein the reagents are labeled without the use of an affinity group, and where the differential isotope labeled reagents result in differential isotope labeled derivatives of the molecules;

(ii) combining the derivatives of the molecules for examination by mass spectrometry; and

(iii) examining the derivatives of the molecules by mass spectrometry. a sample according to the steps recited in any one of claims 1, 2 or 3.

Claim 28 (withdrawn-currently amended) A kit comprising differential isotope labeled reagents and instructions to follow the methods of quantitative analysis of any of claims claim 1, 2 or 3.

Claim 29 (currently amended) A method for the quantitative analysis of two or more derivatives of molecules, wherein the molecules have an amine bearing an active hydrogen and the molecules are derivatized prior to analysis, and wherein the molecules come from two ore more cellular extracts comprising molecules having an amine bearing an active hydrogen, comprising:

(i) reacting the molecules of the extracts with differential isotope labeled reagents, wherein the reagents are ~~directly~~ labeled without the use of an affinity group, resulting in a reductive alkylation of the amine of the molecules to its alkylamine ~~derivative~~ derivatives of the molecules, such that the alkylamine derivatives from each of the extracts are differentially isotopically labeled;

(ii) combining the ~~derivatives of the~~ extracts;

(iii) separating the derivatives of the molecules in the extracts into fractions;

- (iv) enzymatically cleaving the derivatives of the molecules into fragments;
- (v) separating the fragments;
- (vi) examining the fragments by mass spectrometry; and
- (vii) sequencing the fragments.

Claim 30 (new) Use of a mass spectrometer for the quantitative analysis of a sample of molecules, wherein the molecules have an amine bearing an active hydrogen and wherein the molecules are derivatized prior to analysis, comprising:

- (i) reacting the molecules with isotope labeled reagents, wherein the reagents are labeled without use of an affinity group, and wherein reaction with the isotope labeled reagents results in a reductive alkylation of the amine of the molecules to alkylamine derivatives of the molecules, such that the alkylamine derivatives are isotopically labeled for examination by mass spectrometry; and
- (ii) examining the derivatives of the molecules by mass spectrometry.

Claim 31 (new) Use of a mass spectrometer for the quantitative analysis of two or more samples of molecules, wherein the molecules have an amine bearing an active hydrogen and the molecules are derivatized prior to analysis, comprising:

- (i) reacting the molecules in each sample with differential isotope labeled reagents, wherein the reagents are labeled without use of an affinity group, and wherein the differential isotope labeled reagents result in a reductive alkylation of the amine of the molecules to alkylamine derivatives of the molecules, such that the alkylamine derivatives of each sample are differential isotope labeled;
- (ii) combining the derivatives of the molecules for examination by mass spectrometry; and
- (iii) examining the derivatives of the molecules by mass spectrometry.